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# Glucosinolate Aglucones and Analogues: Insecticidal Properties and a QSAR

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**Abstract:** Naturally occurring aglucones of three glucosinolates (sinigrin, glucotropaeolin, and *epi*-progoitrin) were tested for fumigation activity against the house fly, *Musca domestica*, and the lesser grain borer, *Rhizopertha dominica*. A total of eight natural aglucones were evaluated in the bioassays. Two aglucones of sinigrin showed efficacy against both species which was comparable with that of a commercial fumigant, chloropicrin. None of the aglucones tested was comparable in activity to dichlorvos. Aglucones of glucotropaeolin were also insecticidal, but not to the same level as the sinigrin aglucones. The aglucones of *epi*-progoitrin were only slightly effective as fumigants. A quantitative structure–activity relationship (QSAR) was developed for synthetic analogues of the sinigrin and glucotropaeolin aglucones. An electronic parameter, $\sigma^*$, provided the best predictor of activity in *R. dominica*, whereas a hydrophobicity parameter, $\pi$, best predicted activity in *M. domestica*. © 1998 Society of Chemical Industry

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Key words: glucosinolates; aglucones; insecticide; fumigation; QSAR

## 1 INTRODUCTION

Glucosinolates are secondary plant compounds found in most species of the Cruciferae. They have long been thought to serve the plant in a defensive fashion, releasing a volatile aglucone upon damage to the plant tissues.[1]

Glucosinolate aglucones are of several types. In-depth reviews of aglucone formation exist in the literature.[1–3] Sinigrin and glucotropaeolin can each degrade to a nitrile, an isothiocyanate, or a thiocyanate, depending upon conditions at the time of hydrolysis.[3] *Epi*-progoitrin undergoes slightly different reactions: the nitrile is formed as expected, but the isothiocyanate undergoes a spontaneous cyclization to give 5-vinyloxazolidine-2-thione (goitrin; see Fig. 1), and the thiocyanate is not formed at all.[1]

Considerable knowledge exists regarding the effects of glucosinolates and their aglucones on various arthropods and nematodes. Several publications have provided valuable insights by correlating aglucone content of plant material or extracts to biological effects,[4–7] but few have tested high-purity aglucones directly or in a systematic fashion.[8,9]

This study tested the acute fumigation activity of high-purity naturally occurring aglucones of sinigrin (present in black mustard, *Brassica nigra* (L.) Koch), glucotropaeolin (present in garden cress, *Lepidium sativum* L.) and *epi*-progoitrin (present in crambe, *Crambe abyssinica* Hochst ex R. E. Fries) against two insect species, the lesser grain borer (*Rhizopertha dominica* (F.)) and the common house fly (*Musca domestica* L.). In addition, this study examined a quantitative–

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structure activity relationship (QSAR) for the aglucones of sinigrin and glucotropaeolin, as well as synthetic analogues of them.

## 2 MATERIALS AND METHODS

### 2.1 Compounds

*2.1.1 Solvents*

All solvents were certified grade, purchased from Fisher Scientific, Pittsburgh, PA.

*2.1.2 Sources of natural chemicals*

The structures of the naturally occurring aglucones studied are shown in Fig. 1. The sinigrin aglucones allyl cyanide (**1**) and allyl isothiocyanate (**2**) were purchased from Aldrich Chemical Co., Milwaukee, WI, as were all three glucotropaeolin aglucones: benzyl cyanide (**8**), benzyl isothiocyanate (**9**), and benzyl thiocyanate (**10**). Goitrin (**16**), an aglucone of *epi*-progoitrin, was purchased from Lancaster Synthesis, Windham, NH. Allyl thiocyanate (**3**) was synthesized in our laboratory (see Section 2.1.3, below), and (*S*)-1-cyano-2-hydroxy-3-butene (CHB, **15**) was isolated from plant material (see Section 2.1.4, below) (Table 1).

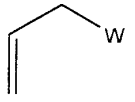
2.1.3 *Synthesis of allyl thiocyanate*

The sinigrin aglucone allyl thiocyanate (**3**) was synthesized from allyl chloride and potassium thiocyanate, using a reaction procedure modified from techniques of Furniss *et al.*[10]

$$H_2C{=}CHCH_2Cl + KSCN \rightarrow H_2C{=}CHCH_2SCN$$

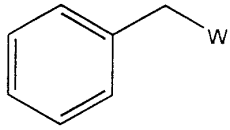
Dimethyl sulphoxide (DMSO, 200 ml) was put into a 1000-ml flask fitted with a reflux condenser and drying tube and stirred with a magnetic stirring bar on a stir plate while KSCN (30 g; 0·31 mol) was added. The mixture was heated to 85°C on a water bath, which was removed when the mixture reached this temperature. Allyl chloride (24·5 ml; 0·30 mol) was added over several minutes. The reaction mixture was allowed to cool and was then washed with four portions of anhydrous diethyl ether (200 ml). The ethereal layer was passed over anhydrous sodium sulfate (to remove water), and the ether was removed with a rotary evaporator at 500 mm Hg vacuum at 25°C. The resulting

Sinigrin aglucones and analogues



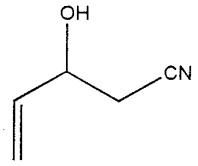

W = CN (**1**)
NCS (**2**)
SCN (**3**)
NCO (**4**)
SH (**5**)
OH (**6**)
$NH_2$ (**7**)

Glucotropaeolin aglucones and analogues

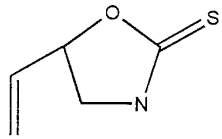



W = CN (**8**)
NCS (**9**)
SCN (**10**)
NCO (**11**)
SH (**12**)
OH (**13**)
$NH_2$ (**14**)

*Epi*-progoitrin aglucones




CHB (**15**)




Goitrin (**16**)

**Fig. 1.** Chemical structures of the glucosinolate aglucones and analogues used in this study.

**TABLE 1**
Names and Sources of Naturally Occurring Glucosinolate Aglucones Used in this Study

| | *Compound* | *Designation*[a] | *Source* |
|---|---|---|---|
| Sinigrin aglucones | Allyl cyanide | **1** | Aldrich |
| | Allyl isothiocyanate | **2** | Aldrich |
| | Allyl thiocyanate | **3** | Synthesis |
| Glucotropaeolin aglucones | Benzyl cyanide | **8** | Aldrich |
| | Benzyl isothiocyanate | **9** | Aldrich |
| | Benzyl thiocyanate | **10** | Aldrich |
| *Epi*-progoitrin aglucones | (*S*)-1-cyano-2-hydroxy-3-butene | **15** | Plant tissue |
| | 5-vinyl-oxazolidine-2-thione (Goitrin) | **16** | Lancaster |

[a] See Fig. 1.

**TABLE 2**
Observed Infrared (IR) and Proton Nuclear Magnetic Resonance ([$^1$H]NMR) Spectra of Allyl Thiocyanate (**3**) Compared with Expected Peaks

| *Spectrum* | *Group* | *Observed* | *Expected*[a] |
|---|---|---|---|
| IR ($cm^{-1}$) | C—H alkene | 3050 | 3049 |
| | C—H alkane | 2960–2880 | 2960–2850 |
| | SCN | 2160 | 2200–2000 |
| | C=C | 1635 | 1640 |
| NMR (ppm) | | 5·8–6·0 (m) 1H | 6·50 1H |
| | | 5·4–5·3 (m) 2H | 5·20 2H |
| | | 3·55 (d) 2H | From 3·19 to 3·25 2H |

[a] Ref. 11.

product was purified by open-column chromatography on silica gel, using hexane + diethyl ether (5 + 1 by volume), collected in 25-ml portions. Thin-layer chromatography was utilized to determine the content of each fraction. Like portions were combined and brought to dryness on a rotary evaporator at the conditions mentioned previously. The observed infrared spectrum and [$^1$H]NMR spectrum (Table 2) of the synthetic product agrees with that expected based on Silverstein *et al.*[11]

*2.1.4 Extraction of* (S)*-1-cyano-2-hydroxy-3-butene* (*CHB*)

(*S*)-1-Cyano-2-hydroxy-3-butene (CHB, **15**), the nitrile aglucone of *epi*-progoitrin, was isolated through Soxhlet extraction of defatted seed meal of *C. abyssinica* (National Sun, Inc., Enderlin, North Dakota). The meal was obtained through the Center for Crops Utilization Research, Iowa State University, Ames, Iowa. Crambe meal (100 g) was placed in the Soxhlet apparatus, and dichloromethane (500 ml) was allowed to cycle through the apparatus by reflux for 24 h at 45°C. The collected dichloromethane was reduced to 50 ml on a rotary evaporator at 500 mm Hg vacuum at 25°C. The organic solution was extracted with water (three volumes), and the water layer was extracted with diethyl ether (three volumes). The ether portions were brought to dryness on a rotary evaporator at the conditions mentioned previously. The resulting product was purified by open-column chromatography on silica gel and hexane + diethyl ether (2 + 3 by volume) solvent system, collected in 25-ml portions. Thin-layer chromatography was utilized to determine the content of each portion. Like portions were combined and brought to dryness on the rotary evaporator. Spectral analysis (Table 3) indicated that the observed infrared spectrograph (IR) of the isolated CHB agreed with that published by Daxenbichler *et al.*[12] and agreed with that expected based on Bellamy,[13] the [$^1$H]NMR spectrum agreed with that published by Das and Torssell[14] and agreed with that expected based on Silverstein *et al.*[11]

The extraction was performed several times to obtain sufficient quantities of CHB.

*2.1.5 Spectroscopic procedures*

All [$^1$H]NMR spectra were obtained in deuterochloroform with tetramethyl silane (TMS) internal standard on a Varian VXR 300. The infrared spectrum of

**TABLE 3**
Comparison of Observed, Published and Expected IR and [$^1$H]NMR Peaks of CHB (**15**)

| *Spectrum* | *Group* | *Observed* | *Published*[a] | *Expected*[b] |
|---|---|---|---|---|
| IR ($cm^{-1}$) | O—H | 3600–3200 | 3450 | 3650–3590 |
| | C—H alkene | 3150 | Bands reported | 3100–3077, 3025–3010 |
| | C—H alkane | 2930 | Bands reported | 2930–2850 |
| | CN | 2270 | 2260 | 2260–2240 |
| | C=C (vinyl) | 1640 | | 1680–1620 |
| NMR (ppm) | | 2·65 (m) 2H | 2·60 (d) 2H | 2·20 1H |
| | | 2·80 (br.s) 1H | 4·0 (br.s) 1H | 2·40 1H |
| | | 4·45 (m) 1H | 4·44 (q) 1H | 4·38 1H |
| | | 5·3 (d) 1H | | 5·20 2H |
| | | 5·45 (d) 1H | 5·1–6·2 (m) 3H | |
| | | 5·90 (m) 1H | | 6·50 1H |

[a] Ref. 12 (IR), Ref. 14 (NMR).
[b] Ref. 13 (IR), Ref. 11 (NMR).

allyl thiocyanate was obtained using a Beckman Acculab 2 with sodium chloride plates, the sample being dissolved in dichloromethane. An infrared spectrum of CHB was obtained on the same apparatus, but by placing a drop of neat sample on a 3M Type 61 Disposable IR card.

*2.1.6 Sources of synthetic analogues*
The following synthetic analogues of natural aglucones, the structures of which are shown in Fig. 1, were purchased from Aldrich: allyl isocyanate (**4**), allyl alcohol (**6**), allyl amine (**7**), benzyl isocyanate (**11**), benzyl mercaptan (**12**), benzyl alcohol (**13**) and benzyl amine (**14**). Allyl mercaptan (**5**) was purchased from Lancaster Synthesis.

*2.1.7 Reference compounds*
Dichlorvos and chloropicrin were tested as reference standards as a basis of comparison in the fumigation-toxicity tests. Both were purchased from Chem Service Inc., West Chester, PA.

*2.1.8 Dilution of chemicals*
For the fumigation tests, all chemicals (except goitrin and benzyl thiocyanate) were dissolved in a commercial brand of corn oil, because acetone proved to be toxic at the levels used for fumigation (data not shown). Benzyl thiocyanate, a crystalline solid, was mixed with corn oil and enough acetone to completely dissolve the crystals. Acetone was not toxic to either *M. domestica* or *R. dominica* at the concentration necessary for solvation of this substance (data not shown). Goitrin and CHB were diluted in pure acetone for use in the topical toxicity test.

## 2.2 Insect bioassays

*2.2.1* Musca domestica *L.* (*Diptera: Muscidae*)
Adult house flies were of the Orlando regular strain, maintained in our laboratory for 14 years.

*2.2.2* Rhizopertha dominica (*F.*) (*Coleoptera: Bostrichidae*)
Adult lesser grain borers were from a colony obtained from the United States Department of Agriculture Agricultural Research Service (USDA-ARS) in Manhattan, KS and maintained in our laboratory for four years.

*2.2.3 Fumigation of* M. domestica
Adult flies (ten) were anesthetized with carbon dioxide and placed into a 50-ml jar supplied with dry food (sucrose + dehydrated milk; 1 + 1 by weight; 1 g) and a length (2 cm) of cotton dental wick wetted with distilled water. The jar was covered with a square of nylon mesh secured with a rubber band. After the flies recovered from anesthesia, three of the small jars were placed into a large amber jar (2·7-litre). A piece of Whatman #4 filter paper was folded in quarters and placed in the bottom of the amber jar with the flies. To the filter paper the appropriate solution of a compound dissolved in corn oil (200 µl) was applied. The jar was securely capped and left undisturbed for the appropriate time period. The jars were then opened and the mortalities recorded. If no observable response (e.g. wing or leg movements) to outside stimuli, such as prodding, was noted, the flies were considered dead.

*2.2.4 Fumigation of* R. dominica
Ten adult beetles were placed in a tube (1·5 × 5 cm) fitted with a metal screen secured by paraffin film, leaving an area open to allow gas exchange. Food (whole wheat kernels, approximately 1 g) was placed in the tube before the introduction of insects. The open end of the tube was then also closed with a metal screen secured with paraffin film, leaving an open area to allow for gas exchange. Three tubes were fastened together, and suspended in a mason jar (490-ml). A piece of Whatman #4 filter paper was folded into quarters and placed in the bottom of the jar. To the filter paper the appropriate corn oil-test compound solution (100 µl) was applied. The mason jars were securely capped and left undisturbed for the appropriate time period. The jars were then opened and the mortalities were recorded. Because this species feigns death, the beetles were considered dead only when they displayed no observable response (e.g. leg or antennal movements) to outside stimuli for $>30$ s.

*2.2.5 Topical application to* M. domestica
Topical application was performed on *M. domestica* for CHB and goitrin only. CHB and goitrin were diluted in acetone, and the appropriate dilution (1 µl) was applied to the thoracic venters of carbon dioxide-anesthetized flies. Mortalities were recorded after 24 h. The flies were considered dead if they displayed no observable response to outside stimuli.

## 2.3 Data analysis

*2.3.1 Calculation of $LC_{50}$ values*
$LC_{50}$ values, expressed as µg (ml air)$^{-1}$, and 95% fiducial limits were calculated using probit analysis on SAS.[15] These were calculated based only on nominal concentrations and assumed 100% volatilization of the compounds in the exposure vessel.

*2.3.2 Regression analysis for QSAR study*
The values of the QSAR parameters Taft's $\sigma^*$ (an electronic parameter) and MR (molar refractivity) were taken from Hansch *et al.*[16] Log *P* values ($\log_{10}$ of the octanol-water partition coefficient, a function of overall hydrophobicity of the molecule) were calculated by

**TABLE 4**
Fumigation $LC_{50}$ Values (μg $ml^{-1}$) of Several Natural Glucosinolate Aglucones and their Analogues, plus Two Commercial Standards

| *Functional group* | *Allyl* | | | | *Benzyl* | | | |
|---|---|---|---|---|---|---|---|---|
| | R. dominica | | M. domestica | | R. dominica | | M. domestica | |
| | *$LC_{50}$* | *95% FL* | *$LC_{50}$* | *95% FL* | *$LC_{50}$* | *95% FL* | *$LC_{50}$* | *95% FL* |
| Cyanide | 2·8 | (2·26, 3·48) | 3·66 | (3·11, 4·10) | 2·37 | (1·93, 2·86) | 0·97 | (0·83, 1·13) |
| Isothiocyanate | 1·57 | (1·47, 1·67) | 0·13 | (0·10, 0·16) | 20·7 | (19·4, 22·6) | 1·17 | (1·00, 1·38) |
| Thiocyanate | 0·55 | (0·50, 0·60) | 0·1 | (0·08, 0·12) | 2·78 | (2·24, 3·45) | 4·27 | (3·68, 5·03) |
| Isocyanate | 2·2 | (2·06, 2·34) | 0·63 | (0·56, 0·70) | 13·8 | (12·0, 15·5) | 5·95 | (4·67, 8·46) |
| Mercaptan | 9·39 | (7·86, 10·36) | 0·25 | (0·20, 0·36) | >21·8 | — | 2·45 | (1·98, 2·95) |
| Alcohol | 7·77 | (7·28, 8·21) | 0·63 | (0·49, 0·71) | >21·9 | — | >7·81 | — |
| Amine | >21·1 | — | >7·52 | — | >23·7 | — | >8·41 | — |
| CHB | >19·6 | — | 6·20 | (4·91, 9·73) | | | | |
| Dichlorvos | 0·29 | (0·21, 0·41) | 0·011 | (0·009, 0·013) | | | | |
| Chloropicrin | 1·3 | (1·20, 1·42) | 0·08 | (0·076, 0·099) | | | | |

using CLogP.[17] The values for $\pi$ (hydrophobicity due to the functional group) were calculated from log *P* values published in Hansch *et al.*[16] and compared with those from the CLogP values via the Hansch–Fujita equation from Chignell:[18]

$$\log P_{\text{fumigant}} - \log P_{\text{propene(or toluene, for benzyls)}} = \pi$$

Log *P* and $\pi$ values for allyl and benzyl isocyanates were not available. All regression equations, $R^2$ values and plotting of the regression curves were calculated by using Microsoft Excel.[19]

## 3 RESULTS

### 3.1 Bioassay results

*3.1.1 Fumigation tests*

The calculated $LC_{50}$ values and 95% fiducial limits for the 24-h fumigation tests are summarized in Table 4. The activities of two commercial fumigants, dichlorvos and chloropicrin, are also shown in Table 4 for comparison. In general, compounds in the allyl series were more toxic than those in the benzyl series, due possibly to the greater volatility of the allyl compounds compared with the benzyls. Some compounds, notably allyl-

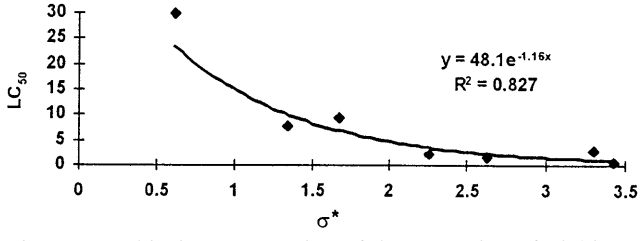



**Fig. 2.** Graphical representation of the regression of $\sigma^*$ (sigma star) on $LC_{50}$ for the allyl compounds in the fumigation test on *Rhizopertha dominica.*

thiocyanate and allyl isothiocyanate, approach chloropicrin in toxicity. Note that the most toxic compounds in either chemical series against either insect species were naturally occurring ones.

*3.1.2 Results of topical applications*

CHB and goitrin were tested topically against *M. domestica* adults. In a preliminary test, CHB displayed modest toxicity, with 55% mortality at 107 μg per fly. Upon further testing, an $LD_{50}$ of 17·4 μg per fly (11·7, 23·0; 95% fiducial limit) was determined for CHB. Goitrin was essentially non-toxic at the levels tested, with 5% mortality at 110 μg per fly, which was not significantly different from a control mortality of 2%.

*3.2.2 QSAR calculations*

A summary of the parameters and $LC_{50}$ values used in QSAR analysis is given in Table 5. $LC_{50}$ values greater than the highest dose tested were set equal to 30 μg (ml air)$^{-1}$ for *R. dominica*, and to 10 μg (ml air)$^{-1}$ for *M. domestica* for purposes of regression calculations. Figure 2 displays a graphical representation of one such regression calculation. The regression equations and coefficients of variation are given in Table 6.

## 4 DISCUSSION AND CONCLUSION

Of the 15 aglucones and analogues tested and shown in Table 4, the most toxic compounds for each series and insect species were naturally occurring. Allyl thiocyanate, from sinigrin, was the most toxic allylic compound to both species, and benzyl cyanide, from glucotropaeolin, was the most toxic benzylic compound

**TABLE 5**
Values for Parameters Regressed against $LC_{50}$ of Both Species

| *Compound* | R. d. $LC_{50}$ | M. d. $LC_{50}$ | $\pi$ | $\sigma^{*a}$ | $MR^a$ | *log* P$^b$ |
|---|---|---|---|---|---|---|
| **1** | 2·8 | 3·66 | −1·37 | 3·3 | 0·63 | 0·4 |
| **2** | 1·57 | 0·13 | 0·17 | 2·62 | 1·72 | 1·94 |
| **3** | 0·55 | 0·1 | −0·8 | 3·43 | 1·34 | 0·97 |
| **4** | 2·2 | 0·63 | — | 2·25 | 0·88 | — |
| **5** | 9·39 | 0·25 | −0·55 | 1·68 | 0·92 | 1·22 |
| **6** | 7·77 | 0·63 | −1·6 | 1·34 | 0·28 | 0·17 |
| **7** | 30 | 10 | −1·7 | 0·62 | 0·54 | 0·07 |
| **8** | 2·37 | 0·97 | −1·17 | 3·3 | 0·63 | 1·56 |
| **9** | 20·76 | 1·17 | 0·44 | 2·62 | 1·72 | 3·16 |
| **10** | 2·78 | 4·27 | −0·74 | 3·43 | 1·34 | 1·99 |
| **11** | 13·84 | 5·95 | — | 2·25 | 0·88 | — |
| **12** | 30 | 2·45 | −0·59 | 1·68 | 0·92 | 2·41 |
| **13** | 30 | 10 | −1·63 | 1·34 | 0·28 | 1·1 |
| **14** | 30 | 10 | −1·64 | 0·62 | 0·54 | 1·09 |

[a] Ref. 16.
[b] Ref. 17.

to both species. For both *M. domestica* and *R. dominica*, allyl thiocyanate was the most toxic insecticide tested. This demonstrates the potential utility of these glucosinolate aglucones as insecticidal fumigants. The high toxicity of allyl thiocyanate and allyl isothiocyanate to these insects is encouraging in the context of biorational insecticides, since these products occur in human foodstuffs, yet are not considered harmful at the concentrations present in foods.[1]

The $LC_{50}$ data reported in Table 4 indicate that two aglucones of sinigrin, allyl thiocyanate and allyl isothiocyanate, are comparable in activity with the commercial fumigant chloropicrin. In fact, against *R. dominica*, allyl thiocyanate surpasses chloropicrin in efficacy, and approaches dichlorvos.

Table 4 and the results of topical application demonstrate that the natural aglucones of *epi*-progoitrin, CHB and goitrin, are modestly toxic to virtually non-toxic; however, a recent publication[7] and other data (unpublished) indicate that the seed meal and extracts of *C. abyssinica* are quite active against insects. Data have yet to be collected to compare the activities of CHB and goitrin to those of other aglucones and commercial fumigants. Perhaps the delivery mechanism is responsible for the discrepancies between the results reported here and those reported previously, because these test methods were not equivalent among the studies. Note, as well, the work of Donkin *et al.*,[20] who concluded that the compound (or compounds) mainly responsible for crambe's toxicity is not a hydrolysis product of *epi*-progoitrin. Further studies will determine if these or other products in crambe meal and its extracts might be exploited as insect control agents.

The toxicities reported correlated well with certain parameters in the QSAR study. We found that clearer relationships were observed, evidenced by larger $R^2$ values, when the allyl and benzyl regressions were calculated separately. For example, from Table 6 in *R. dominica* the value of $R^2$ was 0·549 for $\sigma^*$ when the regression was calculated for all tested chemicals (allyls and benzyls) pooled together. The $R^2$ values increased (0·827 and 0·753) for the allyls alone and the benzyls alone, respectively. A higher $R^2$ value was observed in six out of eight cases for *R. dominica* (this value decreased for MR and $\pi$ when the benzyls were regressed separately) and seven out of eight cases for *M. domestica* (MR stayed roughly equal for the benzyls).

For *R. dominica*, $\sigma^*$ was the best predictor, regardless of whether regressions were calculated for all tested chemicals pooled together, or if the allyl series and benzyl series were analyzed separately. In the tests with *M. domestica*, the $\pi$ parameter best described the toxicity when all tested chemicals were regressed together, as well as when the benzyl series and allyl series analyses were conducted separately.

For the toxicity of the allyls against *M. domestica*, log *P* and $\pi$ have identical $R^2$ values. This is also observed for these two parameters for allyls on *R. dominica*, and the values are close to equal for the benzyls on *R. dominica* and benzyls on *M. domestica*. This is not surprising since both of the parameters are indicators of lipophilicity and, though not strictly equivalent, are closely related through the Hansch–Fujita equation.[16] If either species is used, the $\pi$ parameter may possibly be used interchangeably with log *P* (in the two separate species), depending upon which parameter is more readily available, with little or no loss of predictive accuracy.

At this point, insufficient information is available regarding the bioactivity of these compounds to ascertain specifically why these parameters describe toxicity. Commonly, log *P* and $\pi$ are related to penetration of

**TABLE 6**
Regression Equations and Correlation Coefficients for the QSAR Study

| *Series* | *Species* | *Parameter* | *Regression eqn.* ($y =$) | *Coeff. of Variation* ($R^2$) |
|---|---|---|---|---|
| Allyls | *R. dominica* | $\sigma^*$ | $48{\cdot}1e^{-1{\cdot}16x}$ | 0·827 |
| | | MR | $19{\cdot}7e^{-1{\cdot}82x}$ | 0·460 |
| | | $\pi$ | $1{\cdot}46e^{-1{\cdot}08x}$ | 0·296 |
| | | Log P | $9{\cdot}82e^{-1{\cdot}08x}$ | 0·296 |
| | *M. domestica* | $\sigma^*$ | $3{\cdot}39e^{-0{\cdot}761x}$ | 0·212 |
| | | MR | $6{\cdot}00e^{-2{\cdot}47x}$ | 0·508 |
| | | $\pi$ | $0{\cdot}091e^{-2{\cdot}01x}$ | 0·602 |
| | | Log P | $3{\cdot}22e^{-2{\cdot}01x}$ | 0·602 |
| Benzyls | *R. dominica* | $\sigma^*$ | $98{\cdot}7e^{-0{\cdot}945x}$ | 0·753 |
| | | MR | $18{\cdot}8e^{-0{\cdot}440x}$ | 0·037 |
| | | $\pi$ | $12{\cdot}0e^{-0{\cdot}0414x}$ | 0·0007 |
| | | Log P | $11{\cdot}7e^{0{\cdot}0324x}$ | 0·0005 |
| | *M. domestica* | $\sigma^*$ | $13{\cdot}7e^{-0{\cdot}621x}$ | 0·449 |
| | | MR | $9{\cdot}05e^{-1{\cdot}04x}$ | 0·286 |
| | | $\pi$ | $1{\cdot}47e^{-0{\cdot}892x}$ | 0·471 |
| | | Log P | $16{\cdot}4e^{-0{\cdot}859x}$ | 0·464 |
| Allyls and Benzyls | *R. dominica* | $\sigma^*$ | $84{\cdot}9e^{-1{\cdot}07x}$ | 0·549 |
| | | MR | $25{\cdot}6e^{-1{\cdot}28x}$ | 0·183 |
| | | $\pi$ | $4{\cdot}78e^{-0{\cdot}616x}$ | 0·104 |
| | | Log P | $9{\cdot}11e^{-0{\cdot}0244x}$ | 0·0002 |
| | *M. domestica* | $\sigma^*$ | $9{\cdot}01e^{-0{\cdot}715x}$ | 0·167 |
| | | MR | $10{\cdot}5e^{-1{\cdot}94x}$ | 0·2857 |
| | | $\pi$ | $0{\cdot}43e^{-1{\cdot}49x}$ | 0·365 |
| | | Log P | $3{\cdot}24e^{-0{\cdot}414x}$ | 0·483 |

membranes or to the insect cuticle itself. A parabolic relationship exists in which compounds with log *P* values below a certain threshold cannot penetrate the cuticle or internal lipid membranes, whereas compounds with high log *P* values tend to dissolve and remain within the cuticle or membrane.[18] It may also be possible that certain portions of the molecule associate with certain pockets on macromolecules; for example, the inhibition of bacterial dihydrofolate reductase by 2,4-diaminoquinazolines depends upon the hydrophobicity ($\pi$-value) of the 5-position constituents.[18]

Also, the extent (thermodynamics) of octanol-water partitioning is not linearly correlated to the rate (kinetics).[21] It may be that some compounds with favorable log *P* values cross the membranes too slowly to elicit the effects of other, faster-penetrating compounds with similar log *P* values.

$\sigma^*$ is related to pKa, redox potential, electron density at a remote center, rate of esterification of acids, solvolysis, alkylation of amines,[21] the extent of complex formation with macromolecules[22] and the rate of uptake into the insect's body.[23] All of these functions may be of biological importance.

Finally, many compounds must be activated within the body to be effective, and directly acting electrophiles (those not needing to be activated) are more toxic than unreactive electrophiles (those needing to be activated),[24] regardless of parameter value. More work is needed to determine how these compounds are acting, and how to best employ them as potential insect control agents.

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